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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,946	10/07/2002	Richard J Roman	650053--.91533	8704

7590 03/06/2007

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/937,946	ROMAN ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,7-11,15,17 and 37-44* is/are allowed.

6)☒ Claim(s) *1,7-11,15,17 and 37-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action replaces the Action mailed January 19, 2007, which was withdrawn by the Interview Summary mailed March 1, 2007.

Applicant's Request for Continuing Examination of July 7, 2006, in response to the Final Rejection mailed April 5, 2006, is acknowledged. It is acknowledged that no claims have been cancelled, amended, or added. Claims 1, 7-11, 15, 17, and 37-44 are pending and are hereby reexamined.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Double Patenting

Rejection of Claims 1, 7-11, 15, 17, and 37-44 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-4, 6-13, 19-22, and 24-28 of US Application No. 10/986,695 is maintained. Applicants' state in their response that they "stand ready to address the rejection should it be maintained as an actual rejection".

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Rejection of Claims 1, 7-11, 15, 17, and 37-44 under 35 U.S.C. 112, first paragraph lack of enablement, for the reasons previously explained, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) 20-HETE synthesizing enzymes that are of the CYP4A or CYP4F subclass are known in the art by their amino acid sequences.

(B) Identifying new 20-HETE synthesizing enzyme inhibitors is not part of the instant invention. The invention only calls for the use of known inhibitors or those that will be come known in the future.

(C) The Examiner's argument regarding *Chiron Corp v. Genentech* is not relevant here. In said case, the claims were directed to chimeric antibodies, which was a new technology at the time said applications were filed. Such is not the case in the present application. Known 20-HETE synthesizing enzyme inhibitors are either commercially available or can be readily made.

(D) The gist of the invention resides in the recognition that the four cerebral vascular disease recited in the claims are associated with an increase in 20-HETE level and that inhibitors of CYP4A and CYP4F are effective in treating the diseases. Examples of said inhibitors are disclosed.

(E) Regarding the Examiner's statement that neither 17-ODYA nor miconazole is a specific inhibitor is irrelevant. The relevant point is that said compounds inhibit CYP4A and/or CYP4F and, thus, can be used in the recited method.

(F) Clinical data is not required to enable an invention.

(G) Hoagland et al, 2003 is concerned with hypertension, not one of the four diseases recited in the claims. Clarification of the relevance of Hoagland et al is requested.

These arguments are not found, or are found, to be persuasive for the following reasons. It is acknowledged that

(A) Reply: For the full scope of the recited invention to be practiced, either the specification or the prior art, at the time of filing, must enable the recited invention (MPEP 2164.05(a) [R-2]). Neither the specification nor the prior art enable the skilled artisan to make and use the full scope of treating the recited cerebral vascular diseases with any inhibitor of any CYP4A or any CYP4F enzyme, wherein in the inhibitor has any structure and, wherein the enzyme has any structure. It is acknowledged that the specification teaches that HET0016 is an inhibitor of CYP4A11 and CYP4F2 (Fig 11). It is also acknowledged that the art teaches that DDMS is an inhibitor of HETE synthesis by CYP4A1 and CYP4A3 enzymes (Wang et al, 1998; pg 971, parg 2). Because, only a few examples of an inhibitor of CYP4F have been disclosed, the skilled artisan is not in possession of sufficient guidance to make and use any inhibitor of CYP4F. Furthermore, HET0016 has been shown to inhibit only a single member of each of the CYP4A subtype of HETE synthesizing enzymes, CYP4A11. DDMS is the only compound that has been shown to inhibit more that a single member of the CYP4A subfamily. Based on such teachings, neither the prior art nor the specification provide sufficient guidance to enable the skilled artisan to make and use a method of treatment using any inhibitor of any CYP4A enzyme, wherein in the inhibitor has any structure and, wherein the CYP4A has any structure.

(B) Reply: It is acknowledged that identifying new 20-HETE synthesizing enzyme inhibitors is not part of the instant invention.

MPEP 2164.01(a) states:

> A conclusion of lack of enablement means that, based on the evidence regarding the Wands factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. (Examiner's emphasis)

For a method to be enabled the steps and reagents to be used in order to obtain the desired goal of said method must be provided by the disclosure or the prior art at the time of filing. Applicants' clearly acknowledge that they have not taught the skilled artisan how to practice treatment with any inhibitor of any 20-HETE synthesizing enzyme, as is recited in the claims.

(C) Reply: The instant invention is not limited to known 20-HETE synthesizing enzyme inhibitors.

(D) Reply: It is acknowledged that the current claims are directed to a method of treatment. However, again, in order to practice said method the disclosure must enable the skilled artisan to use the full scope, including any inhibitor of any CYP4A or CYP4F enzyme.

(E) Reply: This argument is found to be valid.

(F) Reply: It is acknowledged that clinical data are not required to enable an invention.

(G) Reply: Hoagland et al, 2003 was cited to support the argument that the specification fails to identify the target population to be treated. This argument is withdrawn since, the claims recite treatment of a patient or animal with occlusive stroke, hemorrhagic stroke, cerebrovasospasm associated with hemorrhagic stroke, and accumulation of blood in sub-arachnoid space caused by head injury.

For these reasons and those presented in the prior actions, rejection of Claims 1, 7-11, 15, and 17, and 37-44 under 35 U.S.C. 112, first paragraph, lack of enablement, is maintained.

Written Description

Rejection of Claims 1, 7-11, 15, and 17, and 37-44 under 35 U.S.C. 112, first paragraph, written description, for the reasons previously explained, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following argument.

(H) The gist of the invention resides in the recognition that the four cerebral vascular disease recited in the claims are associated with an increase in 20-HETE level and that inhibitors of CYP4A and CYP4F are effective in treating the diseases. Examples of said inhibitors are disclosed.

This argument is not found to be persuasive for the following reasons.

(H) Reply: It is acknowledged that the current claims are directed to a method of treatment. However, for the reasons described in the actions of July 14, 2005 and April 5, 2006, the disclosure fails to describe said method in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the full scope of the claimed invention.

For these reasons and those presented in the prior actions, rejection of Claims 1, 7-11, 15, and 17, and 37-44 under 35 U.S.C. 112, first paragraph, written description, is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of Claims 1, 17, 37, 39, and 41 under 35 U.S.C. 102(a), as described in the prior actions, as being anticipated by Alonso-Galicia et al, 1999, as evidenced by Wang et al, 1998 is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following argument. That, Alonso-Galicia et al, 1999 teach intra-cerebroventricular injection of DDMS reduces "cerebral blood flow increase". However, the current claims recite using said inhibitor to increase or prevent a decrease in cerebral blood flow, which is completely different. This argument is not found to be persuasive for the following reasons. As acknowledged by Applicant, Alonso-Galicia et al, 1999 teach intra-cerebroventricular injection of the HETE synthesizing inhibitor DDMS. For rejection of Claims 1, 17, 37, 39, and 41 under 35 U.S.C. 102(a), the purpose of said injection is irrelevant; it is only necessary for the prior art to teach the same method. Any effect of the method is inherent to the method itself. For these reasons and those presented in the prior actions, rejection of Claims 1, 17, 37, 39, and 41 under 35 U.S.C. 102(a) as being anticipated by Alonso-Galicia et al, 1999, is maintained.

Rejection of Claims 1, 37, 39, and 41 under 35 U.S.C. 102(b) as being anticipated by Su et al, 1999, as evidenced by Fotherby et al, 1997 or Schmidt et al, 2000, as described in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments. Su et al, teach that 1-ABT is a 20-HETE inhibitor able to lower blood pressure in hypertensive rats. Sue et al do not show that 1-ABT is able to lower blood pressure in normo-tensive rats. Furthermore, it is not true that lowered blood pressure is an effective treatment for stroke. This argument is not found to be persuasive for the following reasons. As acknowledged by Applicant, Su et al teach treatment with a 20-HETE inhibitor. For rejection of Claims 1, 37, 39, and 41 under 35 U.S.C. 102(a), the purpose of said treatment is

irrelevant; it is only necessary for the prior art to teach the same method. Any effect of the method is inherent to the method itself. For these reasons and those presented in the prior actions, rejection of Claims 1, 37, 39, and 41 under 35 U.S.C. 102(b) as being anticipated by Su et al, 1999, is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of Claims 1, 15, 37, and 39-41 under 35 U.S.C. 103(a) as being unpatentable over Roman et al, 1999 in view of Frisbee et al, 2000, for the reasons previously described, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(I) Roman et al disclose the use of a 20-HETE antagonist, not a 20-HETE synthesis inhibitor.

(J) Neither Roman et al nor Frisbee et al disclose that the increase in 20-HETE level in stroke is caused by increased synthesis rather than release from storage pools. Therefore, it is not obvious to a person of ordinary skill in the art that a 20-HETE synthesizing enzyme inhibitor will work.

These arguments are not found to be persuasive for the following reasons.

(I) Reply: It is acknowledged that Roman et al disclose the use of a 20-HETE antagonist, not a 20-HETE synthesis inhibitor. As previously stated, it is Frisbee et al who teach use of a 20-HETE synthesis inhibitor (pg H1518, parg 4-5).

(J) Reply: It was known in the art, at the time of filing, that cerebral mirovessels produce 20-HETE and that a 20-HETE synthesizing enzyme inhibitor reduces levels of 20-HETE and increases the activity of the K^+ channel (Harder et el, 1994; IDS). Therefore, the skilled artisan would believe that, more likely than not, other effects of 20-HETE would be inhibited by a 20-HETE synthesis inhibitor.

For these reasons and those presented in the prior actions, rejection of Claims 1, 15, 37, and 39-41 under 35 U.S.C. 103(a) as being unpatentable over Roman et al, 1999 in view of Frisbee et al, 2000, is maintained.

Rejection of Claims 1, 15, and 37-43 under 35 U.S.C. 103(a) as being unpatentable over Roman et al, 1999 in view of Powell et al, 1998 or Lasker et al, 2000, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the same arguments described above for the rejection of Claims 1, 15, 37, and 39-41 under 35 U.S.C. 103(a) as being unpatentable over Roman et al, 1999 in view of Frisbee et al, 2000. Applicants are directed to the response above as to why said arguments are not found to be persuasive. For these reasons and those presented in the prior actions, rejection of Claims 1, 15, and 37-43 under 35 U.S.C. 103(a) as being unpatentable over Roman et al, 1999 in view of Powell et al, 1998 or Lasker et al, 2000, is maintained.

There are no new grounds of rejection presented in this Office action. However, the Examiners' response herein is the first rebuttal of Applicants' arguments presented in their response of January 1, 2006. Accordingly, this action is non-final.

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages. It is also requested that Applicants identify support, within the original application, for any amendments to the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Achutamurthy Ponnathapura, can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PRIMARY EXAMINER